The bradykinin B2 Receptor knockout mouse is protected from thrombosis

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Recent investigations in our laboratory propose that the plasma kallikrein/kinin system (KKS) counterbalances the renin-angiotensin system (RAS). The endothelial cell prekallikrein activating enzyme, prolylcarboxypeptidase, also degrades angiotensin II (ATII). This finding along with the fact that the angiotensin converting enzyme (ACE) degrades bradykinin (BK) and forms ATII, plasma kallikrein activates prorenin, BK stimulates tPA, NO, and PGI_2 liberation whereas ATII increases PAI1 and tissue factor levels, and the BKB2 receptor (BKB2R) and angiotensin 1 receptor cross talk intracellularly support that assessment. We sought animal models to examine the interaction between these two systems. Since C1 inhibitor knockout (KO) mice have constitutive intravascular kallikrein formation and BK elevation, we examined whether the absence of BKB2R influenced the time to thrombosis in its KO. BK is the most potent stimulator of tPA liberation *in vivo*; alternatively, the BKB2R accounts for 40% metabolism of BK. The Rose Bengal model for carotid artery thrombosis was established.

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